According to the newly added claims, *inter alia*, the device is used to obtain a volume scan of the breast by synchronously rotating the source and the detector around an axis passing through the breast to form a data acquisition geometry for cone beam volume computed tomography. The three-dimensional tomographic image is formed from the image signals by performing a cone beam volume computed tomography reconstruction on the image signals to produce a three-dimensional attenuation coefficient distribution of the breast. The subject matter of the newly added claims is different from, non-obvious over, and advantageous relative to the subject matter of the applied references, for the reasons set forth below.

A person with ordinary skill in medical imaging would have recognized that *Hsieh* uses a technique called tomosynthesis or limited angle tomography for mammography, as opposed to the newly added claims, which recite a cone beam volume computed tomography (CBVCT) technique for breast imaging. *Hsieh* discloses the use of a cone beam source and a digital detector, but for a limited angle tomographic or tomosysnthesis mammography scan (called Tomosynthesis hereafter). The newly added claims recite the use of a cone beam source and a two dimensional detector for cone beam volume computed tomography breast imaging (CBVCTBI) scan. These two techniques have the following differences:

1. Projection number (different angles): tomosynthesis only needs 2 – 10s projections to perform reconstructions because it deals with only very limited information in a 3D Radon domain or a 3D Fourier domain of the scanned 3D object (a breast in this case). That is why *Hsieh* can have different embodiments consisting of multiple sources on a line or an arc or two detectors. One of his purposes is to provide a system without significantly increasing the cost of such a system (see column 1 and row 40). A system with over 10s x-ray sources will significantly increase the cost of the such system and will be clinically and economically





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unacceptable by the current and the future health systems. CBVCTBI requires hundreds (> 100) of projections on a circle for single circle cone beam geometry or a spiral orbit or hundreds (>100) of circle projections and a few (2-10's) line projections for a circle-plus-line geometry because CBVCTBI intends to acquire a set of projections which cover most of the 3D Radon domain or the 3D Fourier domain of the scanned 3D object (for approximate reconstruction, for example Feldkamp's algorithm), or completely cover the 3D Radon domain or the 3D Fourier domain of the scanned 3D object (for exact reconstruction, for example spiral and circle-plus-line acquisition).

2. Different scanning orbits:

a) In *Hsieh*, the x-ray source and detector are displaced along the x axis for at least two positions while the entire object of interest remains within the field of view (column 1 and line 56-67). The second embodiment is another version of linear tomography with a plurality of stationary x-ray sources and changes the position of the detector in the x-axis (column 2 and lines 6-14). That teaches away from CBVCT, which cannot use a linear orbit alone.

b) In column 4 and lines 30 – 40, *Hsieh* describes an x-ray source rotatable around the y-axis defined in *Hsieh's* patent (column 5 and lines 3-11) describe the detector rotatable around the y-axis to obtain different projection angles. While the reference teaches the general concept of synchronously moving the source and the detector, it does not teach or suggest synchronously rotating the source and the detector around the same axis. In *Hsieh's* independent claims 1, 12, 15, 26, 29, 30, the reference does not describe rotating the x-ray source and the detector around the same axis. In dependent claims 13 and 27 of the reference, even though the reference states that altering the position of the x-ray source and at least one detector array comprise synchronously altering the position of the x-ray source and the position of at least one





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detector array, the reference does not describe rotating the x-ray source and the detector around the same axis syschronously.

c) Circular tomography: the x-ray source or the detector is rotatable around the z-axis defined in *Hsieh's* patent (column 2 and lines 18-20). However, there are no details concerning synchronous rotation. In fact, the circular tomography around the z-axis defined in *Hsieh's* patent can not practically be implemented if the source and the detector rotate synchronously because the patient's body will be in the way of the detector movement. By contrast, the present invention permits, e.g., rotating the x-ray source and the detector synchronously around the longitudinal axis of a breast which passes through the breast and is perpendicular to the chest wall for single circle cone beam orbit to acquire circle projections or rotating the x-ray source and the detector synchronously around the longitudinal axis to acquire over circle projections and displacing the x-ray tube and the detector synchronously along the longitudinal axis of the breast to acquire at least two line projections for a large breast.

3. Different reconstruction algorithms:

The reference has never demonstrated how to reconstruct cross-sectional images from at least two projections. Due to the differences of the two techniques in acquiring projections, two different types of reconstructions algorithms must be used: tomosynthesis uses algorithms which were published in the literature for other applications before *Hsieh's* application was filed, and consists of shifting images and summation. CBVCT uses algorithms which have much more complicated filtering, and 3D backprojection processes and require much heavy computation since it deals with much more data compared to tomosynthesis.

4. Different reconstruction results:





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Digital detector-based tomosynthetic mammography techniques presently under development aim to mitigate the effect of overlapping structures. Though a measure of success will probably be achieved, there still persists a significant amount of missing 3D information that is related to the limited angular range over which projection images are acquired. This indicates that *Hsieh's* technique (tomosynthesis) will result in a series (a few) of images that will still contain a lot of blurring from adjacent planes. In addition, *Hsieh's* technique never achieves isotropic resolution because it is well known that tomosynthesis results in imaging quality which is the Z-axis dependent and scanning geometry dependent (for example, using linear tomography scan which represents the major part of *Hsieh's* patent results in substantially poor image quality for any structures perpendicular to scan direction). CBVCTBI will result in 3D volume reconstruction of 3D distribution of attenuation coefficients of the scanned object (a breast) with isotropic resolution in the x, y and z directions.

Why CBVCTBI is not taught or suggested by the prior art:

1. People used to think that using CBVCT for breast imaging would result in a clinically unacceptable x-ray dose for breast imaging (breast cancer detection). The results of the presnet inventor's computer simulation indicate that CBVCTBI can potentially detect a small (1 mm) carcinoma and a 0.2 mm calcification for an average size breast (10 cm in diameter at the chest wall) with a total dose of 235 mRad. This dose is less than that of a single conventional mammography exam, assuming two views are required for each breast. In addition, the most recent phantom studies confirm that the mean glandular dose level required by the CBVCTBI technique to image an average size breast phantom is less than or equal to that of a conventional mammography exam.





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2. Since CBVCTBI will eliminate structure, CBVCTBI is potentially capable of detecting a 2-3 mm tumor (the inventor has detected an 1.5 mm tumor in his phantom studies), but the average size tumor detectable by mammography is as large as 11 mm. Tomosynthesis will provide some improvement compared to mammography but it is impossible for tomosynthesis to detect such a small tumor. CBVCTBI combined with contrast agent injections, volume growth measurement or angigenesis studies, can potentially be used as a noninvasive diagnostic tool, and for breast cancer treatment planning and monitoring, while both mammography and tomosynthesis mammography are not effective for breast cancer diagnosis, breast cancer treatment planning and monitoring because structures overlap exist in mammography or are not eliminated in tomosynthesis mammography. All these advantages or potential advantages of CBVCTBI are not taught or suggested in the prior art.

To derive the present invention from the prior art, a person would have had to be familiar with both CBVCT and the state of the art of breast imaging strategies and breast cancer detection. Such a person would also have had to appreciate the weaknesses of existing technologies and would have had to appreciate the desirability of combining CBVCT with breast imaging in such a manner as to overcome those weaknesses. As will be seen from the arguments set forth herein, it would not have been straightforward to appreciate or make such a combination.

3. Another challenge of developing CBVCTBI is to develop a practical data acquisition scheme along with accurate and efficient cone beam reconstruction algorithms. The inventor has demonstrated how to achieve a practical data acquisition scheme and what kinds of algorithms for different scan orbits.





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4. Flat panel-based CBVCTBI generates true 3D information with very high resolution which is not available commercially and can not be achieved by fan beam CT (*Redington's* technique) or tomosynthesis (*Hsieh's* technique).

5. Other challenges involve x-ray scatter control and correction techniques to further improve low contrast detectability, as well as an ergonomic design to ensure a targeting CBVCTBI scan and proper coverage of the breast particularly near the chest wall. The pending claims address those challenges.

*Redington* does not overcome the above-noted deficiencies of *Hsieh*. A dedicated fan beam CT mammography imaging scanner for research was previously constructed by GE in the 1970s and clinical trials on the system were performed. A patent was filed by Rowland W. Redington, GE. A dedicated fan beam CT mammography imaging scanner consists of a one-dimensional linear array digital detector (not a 2D area detector) and fan-shaped x-ray (not cone beam detector). Due to then immature CT technology characterized by long scanning time, relatively low spatial resolution and sub-optimal detectors and x-ray techniques, it was not conclusive from the results of those studies whether fan beam CT mammography was superior to conventional mammography. Compared to *Redington's* patent, CBVCTBI will acquire a whole volume within a single scan, instead of scanning slice by slice (column 3 and lines 27-40 in *Redington*) because a fan beam CT mammography device uses a one-dimensional linear array digital detector (not a 2D area detector) and fan-shaped x-ray (not cone beam x-ray ). Therefore, CBVCTBI has three major advantages compared to *Redington's* technique, a) many times faster volume scan (10 –100 times, depending on slice thickness chosen), b) much better spatial resolution due to the use of a two dimensional high resolution detector (this is important for breast imaging to detect both small tumors and microcalcifications) and c) it is able to



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achieve isotropic resolution in the x, y and z directions (fan beam CT mammography can not achieve isotropic resolution because resolution in the direction perpendicular to a slice is generally inferior to that in the slice (the x and y directions ).

CBVCTBI will use cone beam volume CT reconstruction algorithms which are different from those used in fan beam CT mammography. It would not have been obvious to one of ordinary skill in the art to perform the method of *Hsieh* in the device of *Redington* because *Hsieh's* technique would have been recognized as incompatible with that of *Redington.* In addition, the results of the clinical trials performed on the dedicated fan beam CT mammography imaging scanner invented by *Redington* caused many people in medical imaging to believe that CT mammography imaging was not technically superior to current mammography. In addition, the different cone beam volume CT scanning geometries for breast imaging are not well known in the CT art and would not be obvious to one of ordinary skill in the art to use depending on the breast to be imaged because a) no one has used cone beam volume CT for breast imaging before, b) based on the present inventor's research and computer simulation, for different sized breasts, it may be necessary to use different geometries and different cone beam volume CT reconstruction algorithm. For example, using a single circle cone beam volume CT geometry will result in a relative large reconstruction error for a very large sized breast.

While the above arguments are considered to show the patentability of the new claims, the following comments will be submitted with respect to certain ones of the dependent claims.

Regarding claim 90, *Hsieh's* technique (tomosynthesis) will result in (cross sectional) images, each of which still contain blurring from adjacent planes and which is not a true reconstruction of an x-ray linear attenuation coefficient of tissue in the breast. In tomosynthesis imaging, image contrast of a tumor still highly depends on both the size and x-ray linear





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attenuation coefficient distribution of the tumor, like in projection mammography as shown in Table 1 of the present application. However, the present claimed technique reconstructs the 3D distribution of the x-ray linear attenuation coefficient of tissues in the breast. In the CBVCTBI reconstruction image, if the tumor size is bigger than a 5 pixel (voxel) size, image contrast of a tumor only depends on its x-ray linear attenuation coefficient distribution. Thus the image contrast can be represented using the CT number (Table 1). That is why CBVCTBI is potentially capable of detecting a 2-3 mm tumor, while the average size of tumor detectable by mammography is 11 mm. Tomosynthesis is an improvement over mammography; however, theoretically and practically, it is not possible for tomosynthesis to achieve improvement equivalent to or exceeding those of CBVCTBI.

Regarding claim 91, because a carcinoma and a benign tumor have different 3D border patterns, they can potentially be differentiated using ultra-high resolution CBVCTBI which eliminates overlap and presents true 3D images with isotropic resolution. It is proven that mammography has a poor specificity and can not be used for characterizing a tumor. Thus, the present invention provides a significant advantage.

Regarding claim 92, only CBVCTBI can completely eliminate blurring from adjacent planes and truly isolate a plane tomographically from an adjacent plane. *Hsieh's* technique reduces blurring from adjacent planes but it is impossible to eliminate blurring from adjacent planes.

The subject matter of claim 93 would not have been obvious to one of ordinary skill in the art to use in the device of *Hsieh* to measure the volume growth of a breast tumor. Generally, a benign tumor does not grow very fast (most of them do not grow), but carcinomas grow fast. To accurately measure the volume growth of a tumor and determine if it is a carcinoma, it is





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required that a noninvasive imaging technique be capable of accurately reconstructing the tumor. Tomosynthesis mammography is not capable of accurately reconstructing a tumor due to residual blurring from adjacent planes and nonisotropic resolution. However, CBVCTBI is capable of accurately reconstructing a tumor with isotropic resolution and can be very effective in measuring both positive volume growth (for diagnosis of breast cancer) and negative volume growth (for monitoring the effectiveness of therapy).

The subject matter of claims 94 and 95 would not have been obvious because the applied prior art does not eliminate structure overlap and does not provide true reconstruction of 3D linear attenuation coefficients of tissues in a breast, and is therefore not effective for contrast studies and angiogenesis studies. As a consequence, there would have been no motivation to modify the prior art in the direction of claims 94 and 95.

Regarding claim 96, *Hsieh's* device does not provide true 3D description of breast anatomy with high and isotropic resolution which will serve as an accurate 3D coordinate for biopsy procedure. However, the CBVCTBI technique will provide true 3D description of breast anatomy with high and isotropic resolution.

Finally, regarding claims 100-102, *Hsieh* does not teach fast acquisition for a large set of projections and thus provides no motivation to use such a detector. By contrast, the use of such a detector in the present claimed invention permits the elimination of patient motion artifacts as well as contrast studies and angiogenesis studies.

For the reasons set forth above, the Applicant respectfully submits that all outstanding grounds of rejection are overcome and respectfully requests issuance of a Notice of Allowance.

In the event that there are any questions relating to the present Amendment or to the application in general, it would be appreciated if the Examiner would telephone the undersigned



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at the telephone number set forth below concerning any such questions so that prosecution of the present application may be expedited.

Please charge any shortage of fees, or credit any overpayment thereof, to BLANK ROME COMISKY & McCAULEY LLP, Deposit Account No. 23-2185 (000687.00129). In the event that a petition for an extension of time either does not accompany the present Amendment or does not suffice to render the present Amendment timely, the Applicant respectfully petitions under 37 C.F.R. §1.136(a) for an extension of time for as many months as are required to render the present Amendment timely. Any fee due is authorized above.

Respectfully submitted,

Ruola Ning

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